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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/010,914	12/05/2001	Shanker Gupta	9022.30	6114

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EXAMINER
CHOI, FRANK I

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 02/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/010,914	Applicant(s) GUPTA ET AL.	
	Examiner Frank I Choi	Art Unit 1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4,5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Appendix B* .

DETAILED ACTION

Claim Rejections - 35 USC § 112

Claim 18, 19, 22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for non-ionic surfactants, does not reasonably provide enablement for egg phospholipids as nonionic surfactants. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Applicant lists egg phospholipids as non-ionic surfactants, however, the prior art cited indicates that egg phospholipids are ionic surfactants. Applicant does not appear to show how the egg phospholipids are nonionic, as such, it appears that a skilled artisan would be required to do undue experimentation in order to make and/or use a non-ionic egg phospholipid.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/00207 in view of Webb et al. (US 2001/0002404).

WO 00/00207 teaches aqueous parenteral compositions comprising retinoids, such as fenretinide, for the treatment of hyperproliferative disorders (See entire document, especially Pg. 19, lines 13-17).

Webb et al. teach anti-cancer cocktails comprising a mixture of anti-cancer agents such as an anti-cancer drug, a cytokine and/or supplementary potentiating agent(s) are routine in the treatment of cancer, that fenretinide is a known anti-neoplastic agent, and that compositions suitable for parenteral administration conveniently comprise a sterile preparation, such as the combination of polyoxyethylated castor oil and ethanol (Pg. 17, paragraph 0160, Pg. 26, paragraph 0293, Pg. 27, paragraph 0299).

The difference between the prior art and the claimed invention is that the prior art does not expressly disclose the combination of retinides, such as fenretinide, with a solvent comprising an alkoxylated castor oil and alcohol and a method of using the same to treat hyperproliferative disorders. However, the prior art amply suggests the same as fenretinide is known to be used to treat hyperproliferative disorders and that the combination of alkoxylated castor oil and alcohol is a commonly used in parenteral formulations. As such, it would have been well within the skill of and one of ordinary skill in the art would have been motivated to modify the prior art as above with the expectation that combination would be suitable for parenteral delivery of fenrentide and the treatment of hyperproliferative disorders.

Claims 11-18, 20, 21, 23-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lopez-Berestein et al. (US 2002/0143062) in view of Chen et al. (US 6,267,985) and Shudo et al. (US 5,676,146).

Lopez-Berestein et al. teach a method of preparing a liposome by combining N-(4-hydroxyphenyl) retinamide with a phosphatidylcholine, soybean oil, alcohol and water and that typically that liposome are delivered in injectable compositions (Pg. 28, paragraphs 0030,0331, Pg. 29, Paragraph 0340). It is taught that the phosphatidylcholine can be a egg phosphatidyl

choline (Pg. 10, Paragraphs 0081,0089). It is taught that the parenteral aqueous solution should be suitably buffered, if necessary and rendered isotonic (Pg. 29, paragraph 0334). It is taught that retinoids are suitable for the treatment of cancer (Pg. 1, paragraph 0010).

Chen et al. teach that the addition of triglcyerides, such as soybean oil, are conventionally used to increase the solubility of many therapeutic agents (Column 1, lines 10-27, Column 6, lines 17). It is taught that the solubilizers such as ethanol can be added increase the solubility of the therapeutic agent or triglyceride in the composition (Column 33, lines 62-68, Column 34, lines 1-33). It is taught that small particle sizes avoid safety problems found with large particle sizes in parenteral administration (Column 40, lines 26-35). The use of surfactants such as PEG fatty acid esters and POE-POP box copolymers are is taught (Columns 9, 10, Column 20, lines 54-68).

Shudo et al. teach that glycerine is used pharmaceutical formulations for injection as an isotonizing agent (Column 5, lines 47-55).

The difference between the prior art and the claimed invention is that the prior art does not expressly disclose the retinide composition having the claimed components in the claimed amounts. However, the prior art amply suggests the same as the prior art teaches the used of emulsions to administer hydrophobic drugs, including retinoids, for the treatment of cancer. Further, it would have well within the skill of and one of ordinary skill in the art would have been motivated to use a lipid, such as soy bean oil, with the expectation of increasing the solubility of the retinoid, a solvent such as ethanol with the expectation of increasing the solubility of the retinoid and/or lipid, a non-ionic surfactant with the expectation of increasing the ability of the triglyceride to solubilize the retinide. Further, it would have been well within

the skill of one of ordinary skill in the art to use various amounts of the components, including amounts falling within the claimed amounts, depending on the amount of drug, ph, tonicity, stability, solubility and clarity desired.

Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of the references.

Conclusion

A facsimile center has been established in Technology Center 1600. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier numbers for accessing the facsimile machines are (703) 308-4556 or (703) 305-3592.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Choi whose telephone number is (703) 308-0067. Examiner maintains a flexible schedule. However, Examiner may generally be reached Monday-Friday, 8:00 am – 5:30 pm (EST), except the first Friday of the each biweek which is Examiner's normally scheduled day off.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Mr. José Dees, can be reached on (703) 308-4628. Additionally, Technology Center 1600's Receptionist and Customer Service can be reached at (703) 308-1235 and (703) 308-0198, respectively.

FIC
February 8, 2003

JOHN PAK
PRIMARY EXAMINER
GROUP 1600

Appendix B

The following papers have not been made part of the permanent records of the United States Patent and Trademark Office (Office) for this application (37 CFR 1.52(a)) because of damage from the United States Postal Service irradiation process:

Mailroom Stamp Date	Certificate of Mailing Date
7/22/2002	7/9/2002
5/7/2002	4/29/2002

The above-identified papers, however, were not so damaged as to preclude the USPTO from making a legible copy of such papers. Therefore, the Office has made a copy of these papers, substituted them for the originals in the file, and stamped that copy:

COPY OF PAPERS
ORIGINALLY FILED

If applicant wants to review the accuracy of the Office's copy of such papers, applicant may either inspect the application (37 CFR 1.14(d)) or may request a copy of the Office's records of such papers (*i.e.*, a copy of the copy made by the Office) from the Office of Public Records for the fee specified in 37 CFR 1.19(b)(4). Please do **not** call the Technology Center's Customer Service Center to inquiry about the completeness or accuracy of Office's copy of the above-identified papers, as the Technology Center's Customer Service Center will **not** be able to provide this service.

If applicant does not consider the Office's copy of such papers to be accurate, applicant must provide a copy of the above-identified papers (except for any U.S. or foreign patent documents submitted with the above-identified papers) with a statement that such copy is a complete and accurate copy of the originally submitted documents. If applicant provides such a copy of the above-identified papers and statement within **THREE MONTHS** of the mail date of this Office action, the Office will add the original mailroom date and use the copy provided by applicant as the permanent Office record of the above-identified papers in place of the copy made by the Office. Otherwise, the Office's copy will be used as the permanent Office record of the above-identified papers (*i.e.*, the Office will use the copy of the above-identified papers made by the Office for examination and all other purposes). This three-month period is not extendable.